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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,122	01/04/1999	GIULIO TARRO	A31920-PCT-U	7447

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/125,122	TARRO ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,11,13,15,17 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,11,13,15,17 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 26 August 2003 under 37 CFR 1.114 based on parent Application No. 09/125,122 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 26 August 2003 has been entered in full. Claim 21 is added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 7, 9, 11, 13, 15, 17, and 21 are under consideration in the instant application.

Claim Objections

1. Applicant is advised that should claim 7 be found allowable, claim 21 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 103

2. Claims 7, 11, 13, 17, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Bisceglie et al. (New England J Med 321: 1506-1510, 1989) in view of either one of Cummins (U.S. Patent No. 5,824,300) or Cummins et al. (WO 88/03411).

Applicant's arguments (26 August 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the present invention is directed to a peroral method of treating an HCV patient using a liquid formulation of human α-interferon isolated from stabilized lymphoblastoid or leukocytic cell lines. Applicant argues that according to the presence invention, human α-interferon is administered orally at significantly lower doses than is taught by the prior art. Applicant states that in contrast to the claimed invention, Di Bisceglie teaches treating HCV patients with daily subcutaneous injections of approximately one million units of human α-interferon. Applicant submits that the dose taught by Di Bisceglie is 100-200 times greater than the instantly claimed dose. Applicant indicates that Di Bisceglie reports a long-term response rate of 10% (pg 1510, col 1, lines 15-28), which is below the response rate observed when practicing the claimed invention. Applicant argues that in view of the suboptimal results obtained using one million units of human α-interferon, Di Bisceglie recommends administering even higher doses of human α-interferon for longer periods of time. Applicant states that Di Bisceglie points to use of much higher doses than the claimed dose range, which would have cautioned against treating HCV patients by the peroral route with 200 times less human α-interferon than advised by Di Bisceglie. Applicant argues that Di Bisceglie teaches away from the instantly claimed dose range and cannot provide the motivation to combine its teachings with those of Cummins which does not relate to HCV treatment. Applicant adds that Cummins only teaches treating colds, cold sores, AIDS, and warts with low doses for short periods. Applicant contends since Di Bisceglie teaches away from experimentation in the lower dosage ranges, the skilled artisan would not have been motivated to try using the lower doses taught by Cummins, and thus could not have had a reasonable expectation of success. Applicant contends that claimed doses would have been considered ineffective, especially given the state of the art which

demonstrated sub-optimal effectiveness using much higher doses, and the recommendations to push dose levels even higher.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the claims of the instant application do not define a specific patient population that is administered the oral formulation of α-interferon. For example, a "subject" in the claims is interpreted by the Examiner to be any vertebrate that has type C viral hepatitis. In turn, the Examiner has also interpreted that a "subject" could be a mouse, rat, dog, chimp, human, elephant, etc. Therefore, the dosage range of α-interferon recited in the claims is relative to the patient population that it is being administered to. For example, a dosage range of α-interferon of 100 to 500 IU may be considered to be high in a mouse, but low in a human.

Additionally, Di Bisceglie et al. teaches daily subcutaneous administration of human α-interferon to human subjects having type C viral hepatitis. However, each of the Cummins references disclose aqueous formulations of human α-interferon for oral delivery. The Cummins references also teach that for typical patients weighing from about 100 to 225 pounds (*ca.* 45-100 kg), the preferred dosages are thus on the order of 1 to 1125 IU α-interferon per day (0.01 to 5 IU/lb). Among the preferred sources of α-interferon are buffy coat leukocytes ('300, col. 3, lines 25-35; '411, page 4, lines 2-6). Other exemplary formulations described by Cummins contain 1-1500 IU of α-interferon in a dosage volume of one tablespoon (15 ml), or 0.07-100 IU ml^{-1} of syrup ('300 at col. 14, lines 1-5; '411 at page 31, first full paragraph). The Cummins references also disclose that several patient populations are treated with α-interferon, including dogs, cats, and humans ('300, col. 5, lines 1-29; col 8-13; '411, pg 10, 18-29). The Cummins references disclose that disease conditions responding to treatment in accordance with the present invention

may be infectious diseases of viral origin ('300, col 4, lines 66-67; col 5, lines 1-2; '411, pg 10, ¶ 1). Finally, the human patients successfully treated in Cummins are orally administered 0.7 IU/lb of α-interferon twice daily to treat such conditions as rheumatoid arthritis, multiple sclerosis, malignant lymphoma, mesothelioma, and apthous stomatitis ('300, col 12; '411, pg 27-28). For typical patients weighing from about 100 to 225 pounds (*ca.* 45-100 kg), the preferred dosage would thus be on the order of 140 to 315 IU α-interferon per day. The dosages discussed in Cummins overlap with the dosages recited in the instant claims.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a liquid formulation containing 1-1500 IU of human leukocyte α-interferon in a convenient dose delivery volume for oral administration as taught by Cummins to treat a subject having type C viral hepatitis as taught by Di Bisceglie et al. The person of ordinary skill in the art would have been motivated to make that modification because oral delivery of α-interferon (contact with the oral and pharyngeal mucosa) would achieve better results as compared to other forms of delivery, such as intramuscularly or intradermally. The person of ordinary skill in the art would have expected success because human α-interferon was already being administered to subjects with type C viral hepatitis at the time the invention was made. The concentration range claimed by applicant overlaps with the prior art range, and the prior art and the claimed formulations comprise the same active ingredients and are employed in the same manner, i.e., oral delivery in a manner that promotes contact between the liquid α-interferon solution and the oropharyngeal mucosae.

3. Claims 9 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Di Bisceglie et al. and either one of Cummins '300 or '411 as applied to claims 7, 11, 13, and 17 above, further in view of Ratajczak et al. (Arch. Immunol. Ther. Exp. 41: 237-40, 1993).

Applicant's arguments (26 August 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant indicates that Ratajczak et al. discloses the use of lozenges containing 50-100 IU of human lymphoblastoid α-interferon for oropharyngeal delivery to treat patients infected with hepatitis B. Applicant asserts that for the same reasons above regarding Di Bisceglie and Cummins, Ratajczak et al. would not provide any motivation for the skilled artisan to reach the claimed invention. Applicant contends that Ratajczak et al. neither teaches nor suggests use of its α-interferon-containing lozenges to treat HCV.

Applicant's arguments have been fully considered but are not found to be persuasive. Ratajczak et al. is not required to teach all of the limitations of the claims. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare an aqueous formulation of human α-interferon according to Cummins '300 or '411, employing lymphoblastoid α-interferon as described by Ratajczak in place of the buffy coat leukocyte α-interferon noted particularly by Cummins, because Ratajczak evidences that lymphoblastoid interferon was readily available at the time of the invention and teaches that it is suitable for the treatment of an exemplary viral disease *via* delivery to the oropharyngeal mucosae (abstract; pg 237, ¶ 1-2; pg 239) . It consequently would have been obvious to the artisan that lymphoblastoid interferon would be the functional equivalent of the human α-interferon liquid preparations expressly described by Cummins in the '300 and '411 references

for use in the treatment of subjects having type C viral hepatitis as described in Di Bisceglie et al.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
21 October 2003

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER